

Amendment to the Claims:

Please amended the claims and add new claims 73-84 as shown in the listing of the claims below which replaces all prior listings of the claims.

1. to 36. (Cancelled)

37. (Currently amended) A core/shell nanoparticle oligonucleotide conjugate comprising:

(a) a core/shell nanoparticle comprising a magnetic metal-containing core; (b) and a non-alloying gold shell surrounding the core; the gold shell having a predetermined shell thickness and the core/shell nanoparticle having a mean diameter ranging from 5 to 150 nm; and

(eb) oligonucleotides attached to the gold shell, ~~wherein the core of the core/shell nanoparticle does not exhibit a red shifting and broadening of the plasmon resonance band relative to a core surrounded by an alloyed gold shell wherein the non-alloying gold shell is generated on a surface of the core by simultaneous addition of a solution comprising a gold salt and a solution comprising a reducing agent to a solution containing the metal-containing core.~~

38. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the oligonucleotides have a sequence complementary to a portion of a sequence of a target nucleic acid.

39. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of Claim 37 wherein the oligonucleotides include a moiety comprising a functional group which can bind to a nanoparticle.

40. (Currently amended) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the ~~metal-containing magnetic~~ core comprises silver, Pt, Fe, Co, or Ni.

41. (Currently amended) The core/shell nanoparticle oligonucleotide conjugate of claim 40 wherein the ~~core comprises silver~~ predetermined shell thickness is determined by the formula:

$$V_{\text{core}} = 4/3 \pi R^3$$

$V_{\text{core/shell}} = 4/3 \pi (R + A)^3$ wherein A represents the desired shell thickness and R represents the core radius;

$$V_{\text{shell}} = V_{\text{core/shell}} - V_{\text{core}}; \text{ and}$$

$N_{\text{shell}} = d_{\text{shell}} \times V_{\text{shell}} / FW_{\text{shell}}$ wherein N_{shell} represents the amount in moles of gold in the shell, d_{shell} represents 19.3 g/ml, and FW_{shell} represents 196.97 amu.

42. (Currently amended) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the ~~metal-containing magnetic~~ core comprises an alloy metal comprising FePt or FeAu.

43. (Currently amended) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the ~~metal-containing magnetic~~ core comprises a metal oxide.

44. (Cancelled)

45. (Currently amended) The core/shell nanoparticle oligonucleotide conjugate of claim 43 wherein the ~~metal-containing magnetic~~ core comprises Fe_3O_4 or Co_3O_4 .

46. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 37 wherein the gold shell ranges from about 0.5 to about 2 monolayers in thickness.

47. (Currently amended) The core/shell nanoparticle oligonucleotide conjugate of claim 37, wherein the ~~non-alloying gold shell is generated on a surface of the core by simultaneous addition of a solution comprising a gold salt and a solution comprising a~~

reducing agent to a solution containing the metal-containing core results in a reaction mixture having a gold salt concentration of about 2 uM.

48. (Currently amended) The core/shell nanoparticle oligonucleotide conjugate of claim 3747 wherein the gold salt comprises HAuCl₄, NaAuCl₄, KAuCl₄, or KAu(CN)₂.

49. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 48 wherein the gold salt is HAuCl₄.

50. (Currently amended) The core/shell nanoparticle oligonucleotide conjugate of claim 3747 wherein the reducing agent comprises NaBH₄, ascorbic acid, NH₂OH or N₂H₄.

51. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of claim 50 wherein the reducing agent is NaBH₄.

52. (Currently amended) The core/shell nanoparticle oligonucleotide conjugate of Claim 37 wherein nanoparticle-oligonucleotide conjugates ~~are produced which~~ have the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm².

53. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of Claim 52 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm².

54. (Previously presented) The core/shell nanoparticle oligonucleotide conjugate of Claim 53 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm² to about 40 picomoles/cm².

55. (Currently amended) A method for making core/shell nanoparticle oligonucleotide conjugates comprising

(a) providing core/shell nanoparticles comprising metal-containing magnetic cores and non-alloying gold shells surrounding the magnetic cores, the gold shells having a predetermined thickness and the core/shell nanoparticle having a mean diameter ranging from 5 to 150 nm, wherein the cores of the core/shell nanoparticle conjugates do not exhibit a red-shifting and broadening of the plasmon resonance band relative to cores surrounded by alloyed gold shells a core/shell nanoparticle comprising a core and a non-alloying gold shell surrounding the core, the core/shell nanoparticles are prepared by treating the magnetic cores by simultaneous addition of a solution comprising a gold salt and a solution comprising a reducing agent so as to form a reaction mixture having a gold salt concentration of about 2 uM; and

(b) contacting the oligonucleotides with the core/shell nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles;

(c) adding at least one salt to the aqueous solution to create a second aqueous solution; and

(d) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles.

56. (Previously presented) The method of Claim 55 wherein the oligonucleotides include a moiety comprising a functional group which can bind to a nanoparticle.

57. (Previously presented) The method of Claim 55 wherein all of the salt is added to the water in a single addition.

58. (Previously presented) The method of Claim 55 wherein the salt is added gradually over time.

59. (Previously presented) The method of Claim 55 wherein the salt is selected from the group consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of

these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.

60. (Previously presented) The method of Claim 59 wherein the salt is sodium chloride in a phosphate buffer.

61. (Previously presented) The method of Claim 55 wherein nanoparticle-oligonucleotide conjugates are produced which have the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm².

62. (Previously presented) The method of Claim 61 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm².

63. (Previously presented) The method of Claim 62 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm² to about 40 picomoles/cm².

64. (Currently amended) The method of Claim 55 wherein the the magnetic cores comprise a metal oxide, Fe, Ni, Co, FePt or FeAu core/shell nanoparticles are prepared by treating the metal containing magnetic core simultaneously with a solution comprising a gold salt and a solution comprising a reducing agent under conditions that produce a non-alloying gold shell surrounding the nanoparticle cores.

65. (Previously presented) The method of claim 64 wherein the gold salt comprises HAuCl₄, NaAuCl₄, KAuCl₄, or KAu(CN)₂.

66. (Previously presented) The method of claim 65 wherein the gold salt is HAuCl₄.

67. (Previously presented) The method of claim 64 wherein the reducing agent comprises NaBH₄, ascorbic acid, NH₂OH or N₂H₄.

68. (Previously presented) The method of claim 67 wherein the reducing agent is NaBH₄.

69. (Currently amended) A method of detecting nucleic acid bound to a surface comprising:

- (a) providing core/shell nanoparticle conjugates of claim 37;
- (b) providing a surface having nucleic acid bound thereto;
- (c) contacting the nucleic acid bound to the surface with a solution comprising the core/shell nanoparticle oligonucleotide conjugates of claim 37, wherein the nanoparticle core is magnetic, and wherein the contacting takes place under conditions effective to allow hybridization of oligonucleotides bound to the core/shell nanoparticle oligonucleotide conjugates with the nucleic acid bound to the substrate in the presence of with the bound nucleic acid;
- (b) subjecting the nanoparticle conjugate to an external magnetic field so as to accelerate movement of the core/shell nanoparticle oligonucleotide conjugate to the surface to promote interaction hybridization between the nanoparticle conjugate and the nucleic acid;
- (ed) removing from the surface any unbound nanoparticle conjugates that have not hybridized with the nucleic acid; and
- (d) observing a detectable change brought about by hybridization of the nucleic acid with the nanoparticle conjugates.

70. (Previously presented) The method of claim 69 wherein the core/shell nanoparticle oligonucleotide conjugate comprises Fe₃O₄/gold core/shell nanoparticles.

71. (Previously presented) The method of claim 69 wherein step (c) is performed by rinsing the surface with a wash solution or reversing the magnetic field.

72. (Cancelled)

73. (New) The method of claim 69 wherein the magnetic core comprises Fe, Co, or Ni.

74. (New) The method of claim 69 wherein the magnetic core comprises an alloy metal comprising FePt or FeAu.

75. (New) The method of claim 69 wherein the magnetic core comprises a metal oxide.

76. (New) The method of claim 69 wherein the magnetic core is magnetic.

77. (New) The core/shell nanoparticle oligonucleotide conjugate of claim 69 wherein the magnetic core comprises Fe_3O_4 or Co_3O_4 .

78. (New) The method of claim 69 wherein the gold salt comprises HAuCl₄, NaAuCl₄, KAuCl₄, or KAu(CN)₂.

79. (New) The method of claim 78 wherein the gold salt is HAuCl₄.

80. (New) The method of claim 69 wherein the reducing agent comprises NaBH₄, ascorbic acid, NH₂OH or N₂H₄.

81. (New) The method of claim 80 wherein the reducing agent is NaBH₄.

82. (New) The method of Claim 69 wherein nanoparticle-oligonucleotide conjugates are produced which have the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm².

83. (New) The method of Claim 82 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm².

84. (New) The method of Claim 83 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm² to about 40 picomoles/cm².

85. (New) The method of claim 69 wherein the predetermined shell thickness is determined by the formula:

$$V_{core} = 4/3 \pi R^3;$$

$V_{core/shell} = 4/3 \pi (R + A)^3$ wherein A represents the desired shell thickness and R represents the core radius;

$$V_{shell} = V_{core/shell} - V_{core}; \text{ and}$$

$N_{shell} = d_{shell} \times V_{shell} / FW_{shell}$ wherein N_{shell} represents the amount in moles of gold in the shell, d_{shell} represents 19.3 g/ml, and FW_{shell} represents 196.97 amu.